REMARKS

35 USC §103

Reconsideration and withdrawal of the rejection of claims 1-4 and 8-18 under 35 U.S.C. § 103(a) as being unpatentable over Wilhelm (US 2003/00113723) are respectfully requested.

At the outset, it is noted that US 2003/00113723 is believed not to be available as prior art against the present application, because the filing date (July 26, 2002) and the publication date (January 16, 2003) of US 2003/00113723 are subsequent to the June 11, 2002 filing date of the German priority application, DE 102 25 876.7, underlying the present application. The corresponding PCT publication of Wilhem (WO 00/004954), was published on February 3, 2000, more than one year before the priority date of the present application. Applicant has submitted an IDS with a copy of WO 00/004954 concurrently herewith. Further references to "Wilhelm" below encompass both US 2003/00113723 and WO 00/004954.

Applicant respectfully traverses the Examiner's rejection of claims 1-4 and 8-18 as unpatentable over Wilhelm. The Examiner suggests that Wilhelm teaches "structurally similar" compounds to those claimed in the present invention. Applicants respectfully disagree. The compounds disclosed in Wilhelm are quite different from the compounds recited in present claims 1-4 and 8-18. Like the compounds of WO 00/17158 addressed in the Office Action dated August 3, 2007, the compounds of Wilhelm are all amidino compounds (*i.e.*, they all have the $C(NH)(NH_2)$ substituent on the phenyl ring), whereas the presently claimed compounds are all guanidino compounds having the $NH\text{-}C(NH)NH_2$ substituent on the phenyl ring. Even with

Wilhelm in hand, one of ordinary skill would not be led to substitute a guanidino group for the amidino group. There is no suggestion from Wilhelm that one would expect guanidino compounds to be treatments for any of the tumors or lymphomas discussed by Wilhelm. Wilhelm suggests many variables in other portions of the molecule, but all of the compounds contain the amidino group, with no suggestion of variation at that point. It is respectfully submitted that it is only in hindsight with the benefit of the present applicant's specification can it be said to be obvious to modify the Wilhelm compounds as posited.

Moreover, even if there were motivation in the art to substitute a guanidino group for an amidino group, one would still not have the necessary expectation of success after the modification was made. Wilhelm does not provide any structure/activity link between amidino and guanidino groups in the context of treating tumors or lymphomas.

Moreover, even if Wilhelm made out a *prima facie* case of obviousness (which it does not), compounds according to the present claims exhibit a surprisingly high selectivity for urokinase compared to plasmin and thrombin. The Examiner's attention is respectfully directed to the two Sperl declarations previously submitted (on September 5, 2007 and November 29, 2007). Dr. Sperl determined the *in-vitro* inhibition of urokinase, plasmin and thrombin by two compounds according to the present invention and compared the results to data for a corresponding amidino compound. (1st Dec. at ¶ 4-5; 2d Dec. at ¶ 4.) The compounds of the present invention were both highly selective for urokinase, as compared to plasmin and thrombin. (1st Dec. at ¶ 4; 2d Dec. at ¶ 5.) Dr. Sperl contrasts those data with the data in the Pentapharm Product Catalog 1998 for 3-amidino compounds. (1st Dec. at ¶ 5.) He concludes, based on the

published data for those compounds, that the amidino compounds are much less selective for urokinase compared to plasmin and thrombin. (*Id.*) Dr. Sperl also ran a set of experiments in parallel in which Ki measurements were made on two compounds according to the present invention (WX-682 and WX-684) as well as the Pefabloc® uPA compound from the Pentapharm Product Catalog 1998 (WX-UK1). (2d Dec. at ¶ 4.) The compounds of the present invention were more highly selective for urokinase as compared to plasmin and thrombin than was the corresponding amidino compound. (*Id.*) Dr. Sperl concludes that the high selectivity of the presently-claimed guanidino compounds is surprising and unexpected (1st Dec. at ¶ 5; 2d Dec. at ¶ 4.) It is respectfully submitted that one of ordinary skill would find the high selectivity of the guanidino compounds surprising and unexpected.

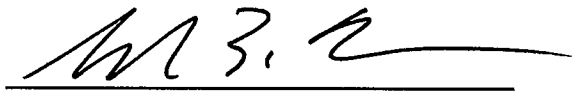
Thus, for all of the foregoing reasons, the rejection under §103 should not be maintained.

Double Patenting

Claims 1-4 and 8-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 28-49 and 53-58 of copending Application No. 10/521,805 filed January 21, 2005. Because this is a provisional rejection; the claims in SN 10/521,805 have not been allowed; and the claims in this application are otherwise ready for allowance; the present rejection should be withdrawn.

It is believed that the present case is in condition for allowance, and a favorable Action is respectfully requested.

Respectfully submitted,



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